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PATENT

Attorney Docket No.: 15631-000480US
Client Docket No.: DX0758K1RE

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of J. Fernando Bazan	Examiner: Joseph F. Murphy, Ph.D.
Application No.: 09/935,366	Art Unit: 1646
Filed: August 22, 2001	
For: DNA ENCODING INTERLEUKIN-B30	**Response to Office Action**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in response to the "final" Office Action mailed June 12, 2002 in the above-captioned patent application. Reconsideration is respectfully requested in view of the following remarks. A precautionary notice of appeal and the appropriate fees accompany this response.

Status of the Application

Claims 1-7, 9-10, and 12-17 are pending and stand rejected in the application. The claims remain rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as allegedly lacking utility. These rejections, the only outstanding issue in the subject application, are addressed below.

Rejections under 35 U.S.C. 101 and 35 U.S.C. 112, 1st Paragraph

The instant Office Action maintained the rejection of the pending claims as allegedly lacking apparent or disclosed patentable utility. Applicant has previously pointed out that, contrary to the assertions of the Office, the subject specification has disclosed patentable

utility in the present application that is substantial, specific, and credible. Applicant also noted that the disclosed utilities were further confirmed and experimentally verified in peer viewed publications. In response, the instant Office Action maintained that effects of the sequence differences on protein structure and function cannot be predicted. The Office Action stated that the specification "essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide." The Office Action also noted that assays disclosed in the specification for measuring IL-B30 expression and function is credible and substantial but not specific. The Office Action further stated that the publications previously noted by Applicant all require that IL-B30 associates with IL-12 p10 to function, which was not disclosed in the specification, and therefore cannot be used to establish the utility of the claimed polynucleotide. Applicant respectfully traverses the instant rejection for the reasons stated below.

1. Reiteration of legal standard for the utility requirement

Applicant first notes that, according to the MPEP (§ 2107.02 III-A), a disclosed utility corresponding to the claimed subject matter satisfies the utility requirement under § 101 absent evidence which would cast doubt on the objective truth of the disclosed utility. There is no legal requirement that the disclosed utility must be supported by conclusive experimental results. The MPEP has noted that several judicial decisions "direct the office to presume that a statement of utility made by an applicant is true." As quoted in the MPEP:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope. [MPEP§ 2107.02-III-A; quoting *In re Langer*, 503 F.2d 1380 (CCPA 1980), at 1391; emphasis original]

The MPEP has also cautioned that "office personnel should not begin an evaluation of utility by assuming that an asserted utility is likely to be false, based on the technical filed of the invention or for other general reasons." Rather, "any inquiry must start by asking if there is any reason to question the truth of the statement of utility" (MPEP § 2107.02-III-A; at page 2100-39).

The MPEP specifically noted that "applicant does not have to provide evidence sufficient to establish that an asserted utility is true 'beyond a reasonable doubt'" and that "nor must an applicant provide evidence such that it establishes an asserted utility as a matter of statistical certainty." See, MPEP § 2107.02-VII. The MPEP further states that "evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true" (MPEP § 2107.02-VII; emphasis original).

In addition, with respect to therapeutic or pharmaceutical utilities, the MPEP indicates that a reasonable correlation between the evidence and the asserted utility is sufficient. As noted in the MPEP, the courts "have routinely found evidence of structural similarity to a compound known to have a particular therapeutic or pharmaceutical utility as being supportive of an assertion of therapeutic utility for a new compound" (MPEP § 2107.03-II; emphasis added).

Further, with respect to the "credible" prong of the utility requirement, the MPEP states that the determination is "whether the assertion of utility is believable to a person of ordinary skilled in the art based on the totality of evidence and reasoning provided." The MPEP further notes that "an assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion" (MPEP § 2107.02-III-B).

Moreover, even if the Office has provided evidence showing that one of ordinary skill in the art would doubt the asserted utility, the applicant can nonetheless submit rebuttal evidence sufficient to convince such a person of the invention's asserted utility (MPEP § 2107.02-V; at page 2100-42).

Finally, Applicant notes that, as stated in the MPEP, "an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112; additional statements of utility, even if not credible," do not render the claimed invention lacking in utility" (MPEP § 2107.02-I; at page 2100-37; emphasis added).

2. Utilities of the subject invention

Applying the above-noted legal standard for utility requirement, there is no doubt that the subject specification has disclosed patentable utilities that are substantial and specific. Other than the structural similarities between IL-B30 and other members of the long chain cytokines, the specification also disclosed that IL-B30 could modulate receptor function as receptor ligands (see, e.g., Col. 11, lines 43-49). The specification taught that IL-B30 can be involved in various cellular activities including inflammation (e.g., Col. 25, lines 55-62), which is supported by actual experimental data disclosed in the specification. **For example, the specification sets forth actual data which demonstrate that IL-B30 is differentially expressed in a number of immune active cells, including activated macrophages or activated dendritic cells (see, Col. 34, lines 35-41). These experimental data indicate that IL-B30 is at least useful as a marker for these immunologically important cell types.**

It was also disclosed in the specification that IL-B30 polypeptides and nucleic acids can be useful for identifying novel cytokine receptors or screening modulators of other cytokines and their receptors (Cols. 30-31). Such utilities are certainly ***substantial*** because they define ***real world*** uses of the claimed subject matter.

The subject specification also taught how to make use of and experimentally confirm the disclosed utilities. As explained in more detail in Applicant's previous response, the specification specifically disclosed how to assay expression level of IL-B30 in various human and mouse cell types (see, e.g., Cols. 32-35). The specification set forth how to experimentally examine other biological functions of IL-B30 (Col. 36, line 65 to Col. 38, line 50). For example, the specification provided detailed procedures for one to assay effects of IL-

B30 on cytokine production (e.g., Col. 37, line 44) or peripheral blood mononuclear cell proliferation (e.g., Col. 38, line 6). It is readily clear that not all polypeptides can regulate cytokine production or play a role in inflammation. Therefore, contrary to the assertion of the instant Office Action, these assays cannot be performed with simply any polynucleotide. Rather, such disclosures of the subject application are ***specific*** because they are specific to the subject matter being claimed.

In this connection, Applicant also respectfully disagrees with the Examiner's assertion that the present invention did not disclose a specific utility because the specification "essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide." As stated in the MPEP, a "specific utility" is specific to the subject matter claimed, which is contrasted with a general utility that would be applicable to a broad class of the invention. The MPEP further explains that non-specific utility exists in "situations where the applicant merely indicates that the invention may prove useful without identifying with specificity why it is considered useful." The examples noted by the MPEP as non-specific utility include "indicating that a compound may be useful in treating unspecified disorders, or that the compound has non-specified 'useful biological properties.'" Similarly, a polynucleotide whose use is disclosed simply as gene probe or chromosome marker would not be considered to be specific. See, MPEP § 2107.01-I, at page 2100-32). As explained in the previous paragraph, the subject invention has disclosed utilities that are clearly distinguished over such non-specific utilities exemplified in the MPEP.

Finally, the disclosed utilities are also ***credible***. First, the subject disclosures as well as knowledge known to the skilled artisans are more than sufficient to satisfy the "more likely than not true" test. In addition, as reiterated below, the disclosed utilities of the subject invention were experimentally confirmed by peer reviewed publications. These publications demonstrated that IL-30B can indeed bind to cytokine receptors and regulates immune responses, and that altered levels of IL-B30 correlate with a number of cellular activities. Significantly, these published studies all employed substantially the same methods and assays

as described in the subject specification. This strongly indicates that the utilities as disclosed in the subject invention would have been regarded as credible by the skilled artisans.

3. Confirmation of the disclosed utilities in post-filing publications

Applicant has provided in the previous response publications which experimentally confirmed the utilities disclosed in the subject specification (Wiekowski et al., J. Immunol., 166: 7563-70, 2001; and Oppmann et al., Immunity, 13: 715-25, 2000). It should be noted that these references were not provided to establish, or as disclosure of, utilities of the subject invention. Rather, they were provided as additional evidence that the utilities already disclosed in the subject specification are substantial and credible. Also, as discussed above, the MPEP clearly indicates that Applicant is entitled to further evidence to rebut any assertion of a lack of utility. The law does not exclude post-filing publications as additional evidence that the utilities already disclosed in the patent application is substantial, specific, and more importantly in the instant case, credible. Rather, the MPEP specifically states that "there is no predetermined amount or character of evidence" an applicant can provide to support an asserted utility, . . ." (MPEP § 2107.02-VII).

It must be emphasized that the post-filing publications do not contradict the disclosed utilities although the subject specification did not expressly teach that IL-B30 is a subunit of IL-23. As discussed above, Applicant needs only to disclose one patentable utility in order to satisfy the utility requirement. It is not necessary for Applicant to disclose all possible utilities or biological function of the IL-B30 protein. In the present case, Applicant has disclosed in the specification various utilities of IL-B30. For example, the specification teaches that IL-B30 can play a role in inflammation and a number of other cellular activities (see, Col. 34, lines 35-41). This is precisely what was experimentally confirmed in the published reports. Specifically, one of previously submitted publications, Wiekowski et al. (J. Immunol., 166: 7563-70, 2001), demonstrated that expression of IL-B30 indeed induces

multiorgan inflammation (see, e.g., the title and abstract). Therefore, the functional properties of IL-B30 disclosed in the subject specification clearly satisfy the utility requirement.

In addition, while Wiekowski et al. and Oppmann et al. disclosed that IL-B30 is a subunit of IL-23, it does not follow that utilities of IL-B30 can be practiced only when it is complexed with other subunits of IL-23. To the contrary, Wiekowski et al. clearly indicate that just alternating IL-B30 expression levels could lead to various cellular and immunological responses in vivo. Such is one of the disclosed utilities of the subject invention, substantial, specific, and credible.

Moreover, even assuming that IL-B30 indeed has to be complexed with IL-12p40 in order to be functional in vivo, this at most relates to the underlying mechanism of the disclosed utility. It is well established that an applicant does not need to show the underlying mechanism of his invention in order to obtain a patent on his invention. Therefore, non-disclosure of IL-B30 being a subunit of IL-23 is simply immaterial to the issue of whether IL-B30 has a patentable utility.

4. Further analysis of the instant rejection

With due respect, Applicant submits that the Office did not meet the initial burden as required by the MPEP (see, e.g., MPEP § 2107.02-IV) in providing evidence to establish a prima facie showing that the claimed invention lacks utility, i.e., evidence that the skilled artisans would not believe that the disclosed utilities are "more likely than not true." Rather, the Office appeared to have taken the position that disclosed utilities are not patentable utility unless accompanied with conclusive experimental proof. In essence, the Office Action is shifting the initial burden to Applicant without first establishing the required prima facie showing.

The instant rejection was maintained partially in view of the discussions of Doerks et al. (Trends in Genetics 14:248-50, 1998); Brenner et al. (Trends in Genetics 15:132-33; 1999); and Bork et al., Cur. Opin. Struc. Biol. 8:331-332, 1998). It was alleged that these

references indicate that amino acid sequence homology cannot necessarily predict the function of proteins. However, Applicant notes that the cited art at most suggested that homology-based functional predictions may not always be accurate. By no means did these references establish that in any given case, sequence homology based functional prediction cannot be "more likely than not true." Thus, the cited art are clearly not evidence that the logic underlying the asserted utility is seriously flawed or that the facts upon which the asserted utility is based are inconsistent with the logic underlying the assertion.

In addition, the references cited by the Examiner all relate to the general technical fields of molecular biology and biochemistry, not specific to the subject matter of the present invention. By contrast, Wiekowski et al. and Oppmann et al. provide scientific evidence specific to the subject invention, i.e., IL-B30. Clearly, the general proposition noted in the references cited by the Examiner cannot refute the specific and actual evidence reported in Wiekowski et al. and Oppmann et al. which confirmed the utilities of IL-B30 as disclosed in the subject invention. Further, the fact the latter employed substantially the same assays and methods as disclosed in the subject specification simply indicate that the disclosed utilities are credible. In light of such actual and specific evidence, it is wholly improper for the Office to resort to a *per se* unpredictability position in dismissing the disclosed utilities of the subject specification.

Further, the subject application disclosed novel nucleic acid sequences and their utilities. The disclosed utilities were based in part upon homology to existing nucleic acids encoding other long chain cytokines which have established utilities. As noted in Applicant's previous response, the Utility Guidelines specifically stated that under such circumstances, "the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." [Utility Examination Guidelines, Federal Register 66 (4) at page 1096]. Consistently, in the Utility Guideline Training Materials, patentable utility is found in the disclosure of Example 10, which is quite analogous to that of the subject application. There, a disclosure of a DNA sequence with substantial

sequence homology to known DNA ligases was found to have patentable utility. Applying the same test, the presently claimed polynucleotide sequences, which share sequence homology and common motifs with the known long-chain cytokines, certainly also have patentable utilities.

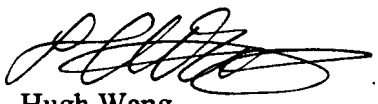
In summary, Applicant submits that the present invention has disclosed patentable utilities that are substantial, specific, and credible. Withdrawal of the instant rejections is respectfully requested.

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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